# Supporting information

## Supplementary figures

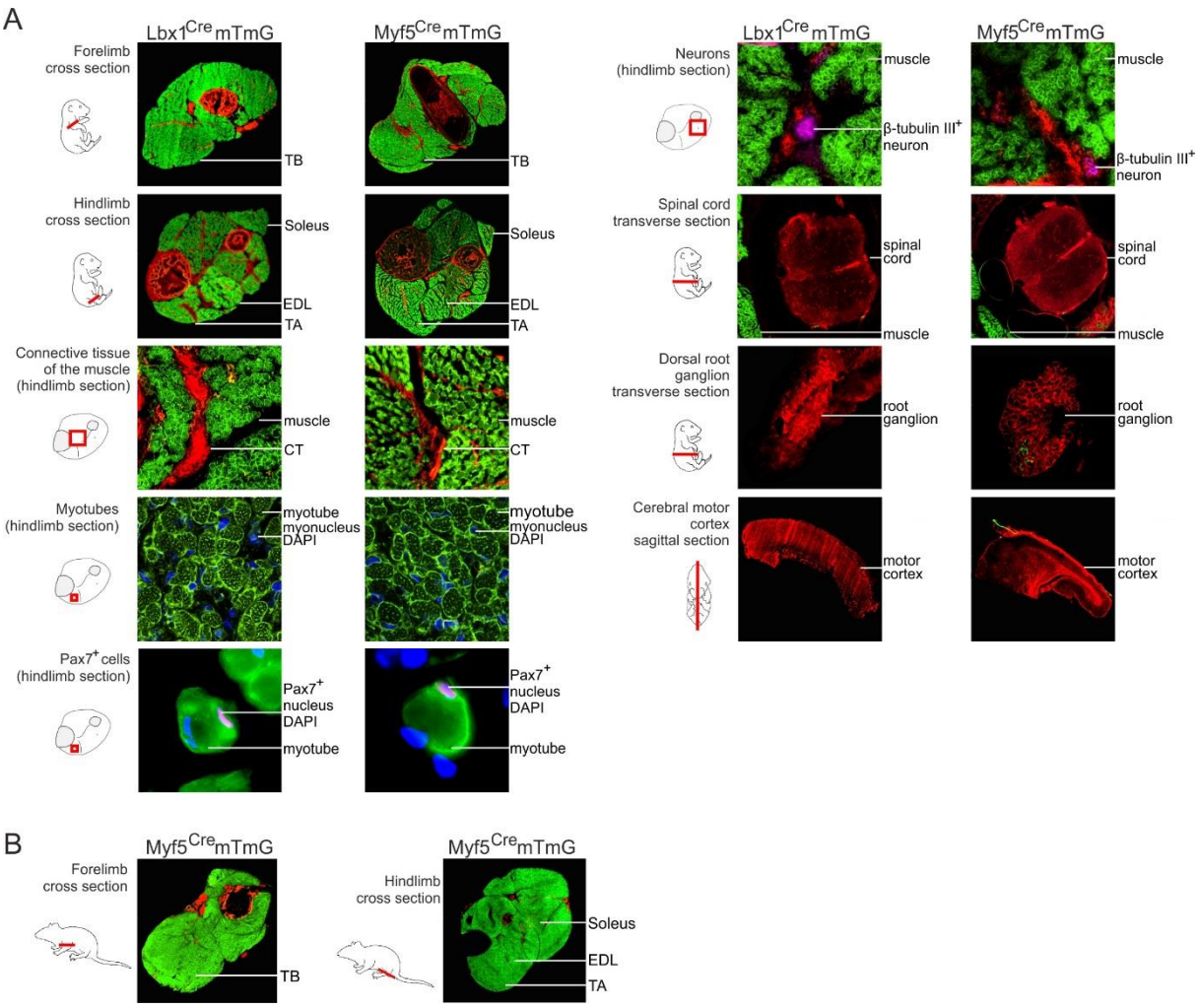


**Fig. S1** Characterization of Lbx1$^{Cre}$ and Myf5$^{Cre}$ specificity (A, B) Analysis of Lbx1Cre and Myf5Cre specificity. Cre mice were bred to Rosa26$^{mTmG}$ reporter mice and analyzed at embryonic day 18 (E18.5; A) or postnatal day 21 (p21; B). Staining: green depicts mG reporter activity tracing recombined cells, red depicts mT reporter activity tracing non-recombined cells. Satellite cells have been stained for Pax7, neurons for β-tubulin III (purple). TB: Triceps brachii; CT: connective tissue; EDL: Extensor digitorum longus; TA: Tibialis anterior.

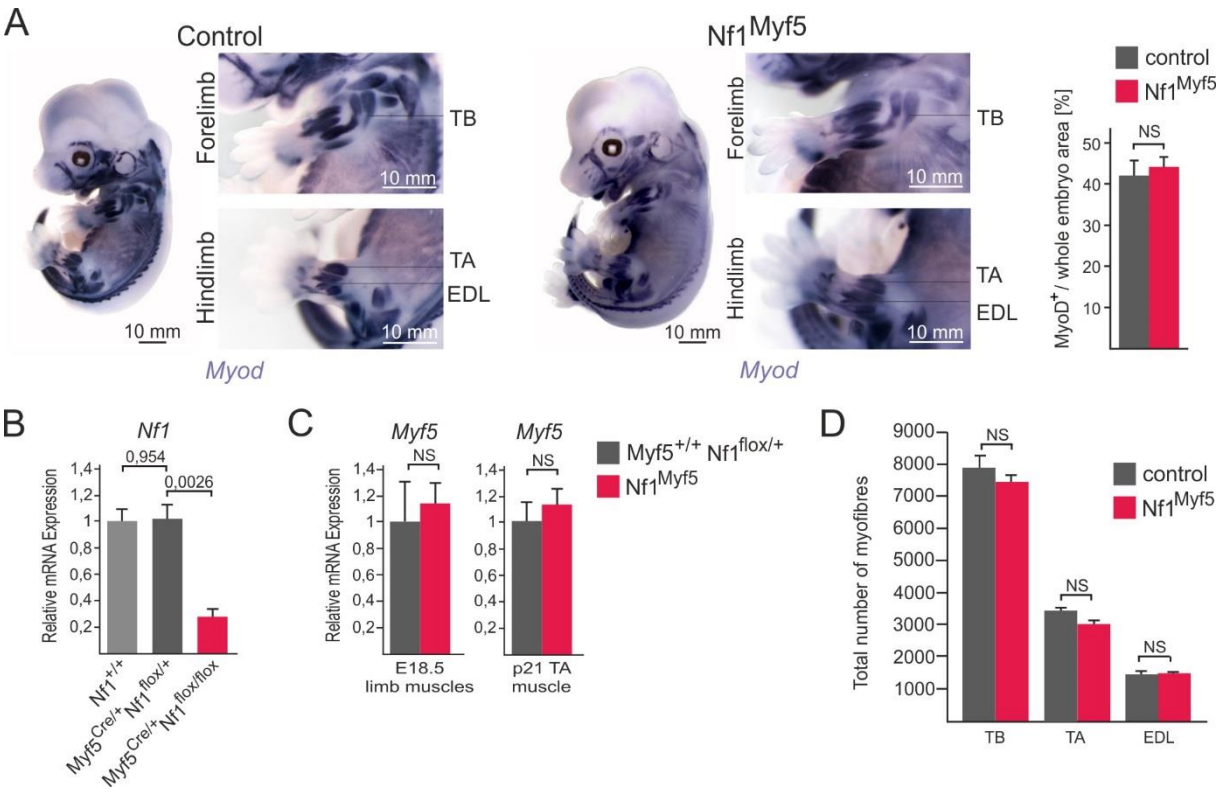


**Fig. S2** Extended data for pre- and postnatal characterization of Nf1$^{Myf5}$ animals (A) Whole-mount *in-situ* hybridization of 14 day old control and Nf1$^{Myf5}$ embryos for *Myod*. Quantification of *Myod*+ area in limbs is shown right (n=3 animals per genotype). **(B) RT-qPCR analysis of *Nf1* expression in p21 Tibialis anterior (TA) muscles of Nf1$^{+/+}$, Myf5$^{Cre}$;Nf1$^{flox/+}$ and Myf5$^{Cre}$;Nf1$^{flox/flox}$ animals (n=3 animals per genotype).** (**C**) RT-qPCR analysis of *Myf5* expression from Myf5$^{+/+}$;Nf1$^{flox/+}$ vs. Myf5$^{Cre/+}$;Nf1$^{flox/flox}$ animals in E18.5 limb muscles and p21 TA muscle (n=3 animals per genotype). (**D**) Quantification of total myofiber numbers in muscles (TB: Triceps brachii, TA: Tibialis anterior, EDL: Extensor digitorum longus) of p21 control and Nf1$^{Myf5}$ animals (n=3 animals per genotype). **Error bars represent standard error of means (SEM). P-value was calculated by two-sided unpaired t-test. P-value above 0,05 was considered not significant (N.S.).**

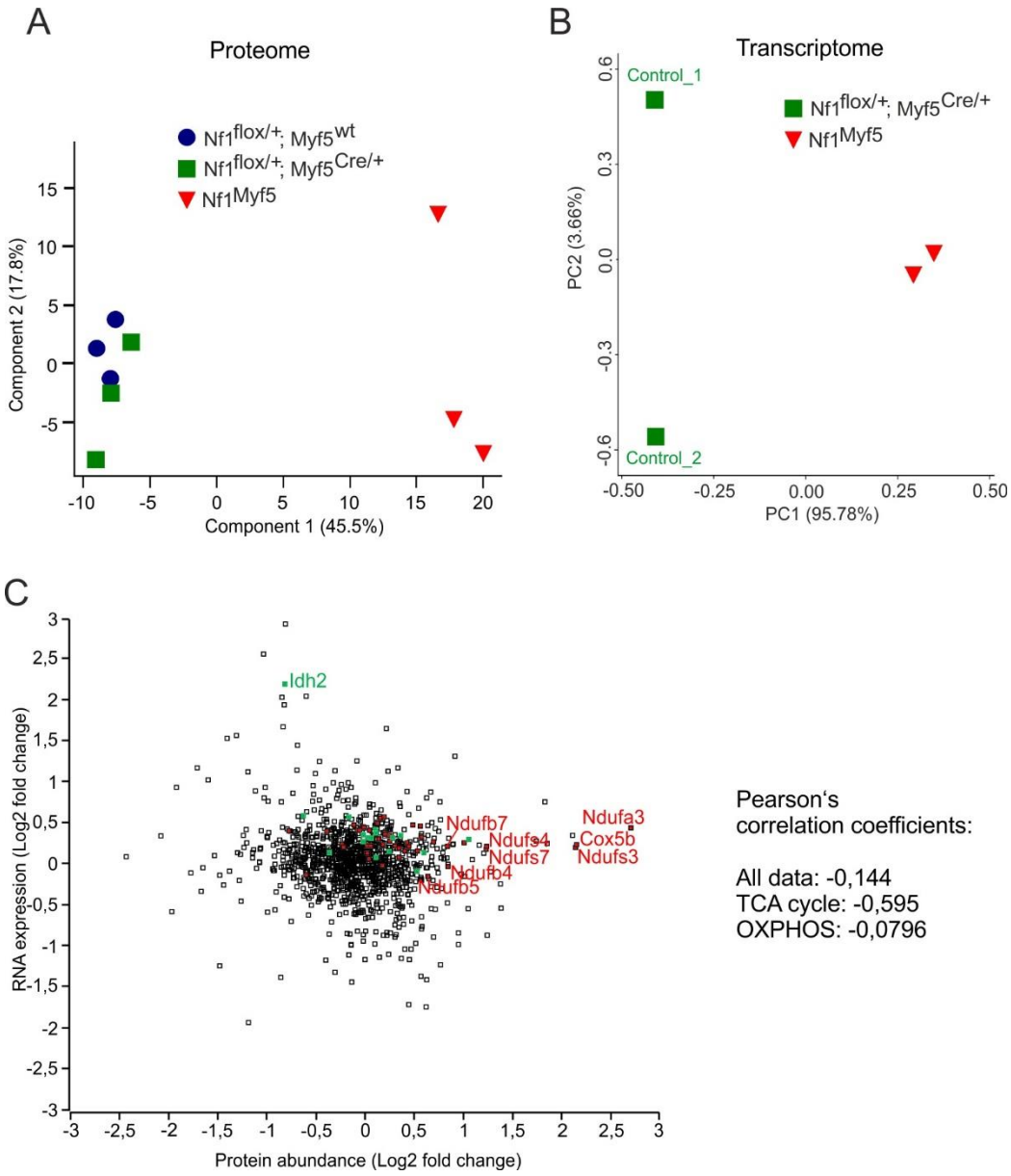


**Fig. S3** Extended data proteome and transcriptome analysis (A, B) Principal component analysis (PCA) of proteome (A) and transcriptome (B) data. Genotypes are indicated. **(C) Correlation analysis of transcriptome and proteome data. The Pearson correlation coefficient between transcript and protein levels of Nf1Myf5 and control TA muscles are shown as a log2-fold change (all squares, -0.144). Specific factors involved in the ETC (red, -0.0796) and the TCA cycle (green, -0.595) are highlighted. Pathway identities were retrieved from KEGG.**

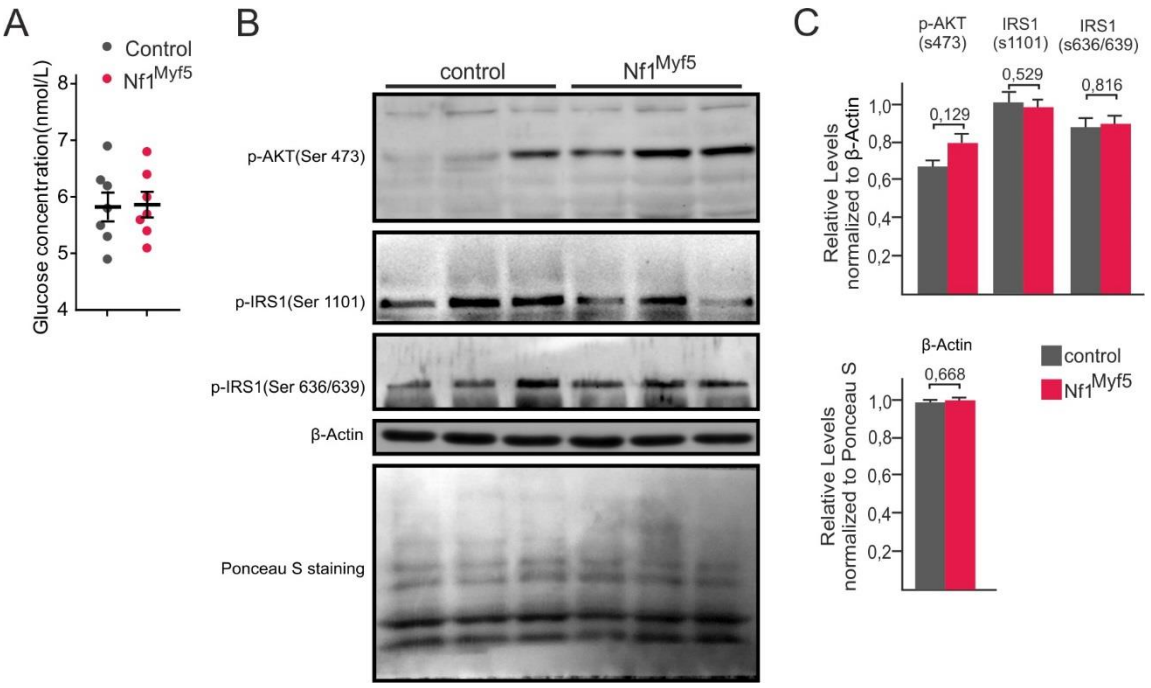


**Fig. S4** Blood glucose and insulin signaling in Nf1$^{Myf5}$ mice (A) Blood glucose test in 5 weeks old Nf1$^{Myf5}$ animals (n=7 animals per genotype; each dot represents measurement from one individual animal). (B) Western blot analysis for phosphorylated AKT (Ser473) and phosphorylated IRS1 (Ser1101, Ser 636/639). **(C) Quantification of p-AKT(s473), p-IRS1(s1101) and p-IRS1(s636/639) relative to β-actin levels (top); bottom: β-actin was equally abundant in control and Nf1$^{Myf5}$ samples, measured relative to Ponceau S staining (n=3 animals per genotype). Error bars represent standard error of means (SEM). P-value was calculated by two-sided unpaired t-test.**

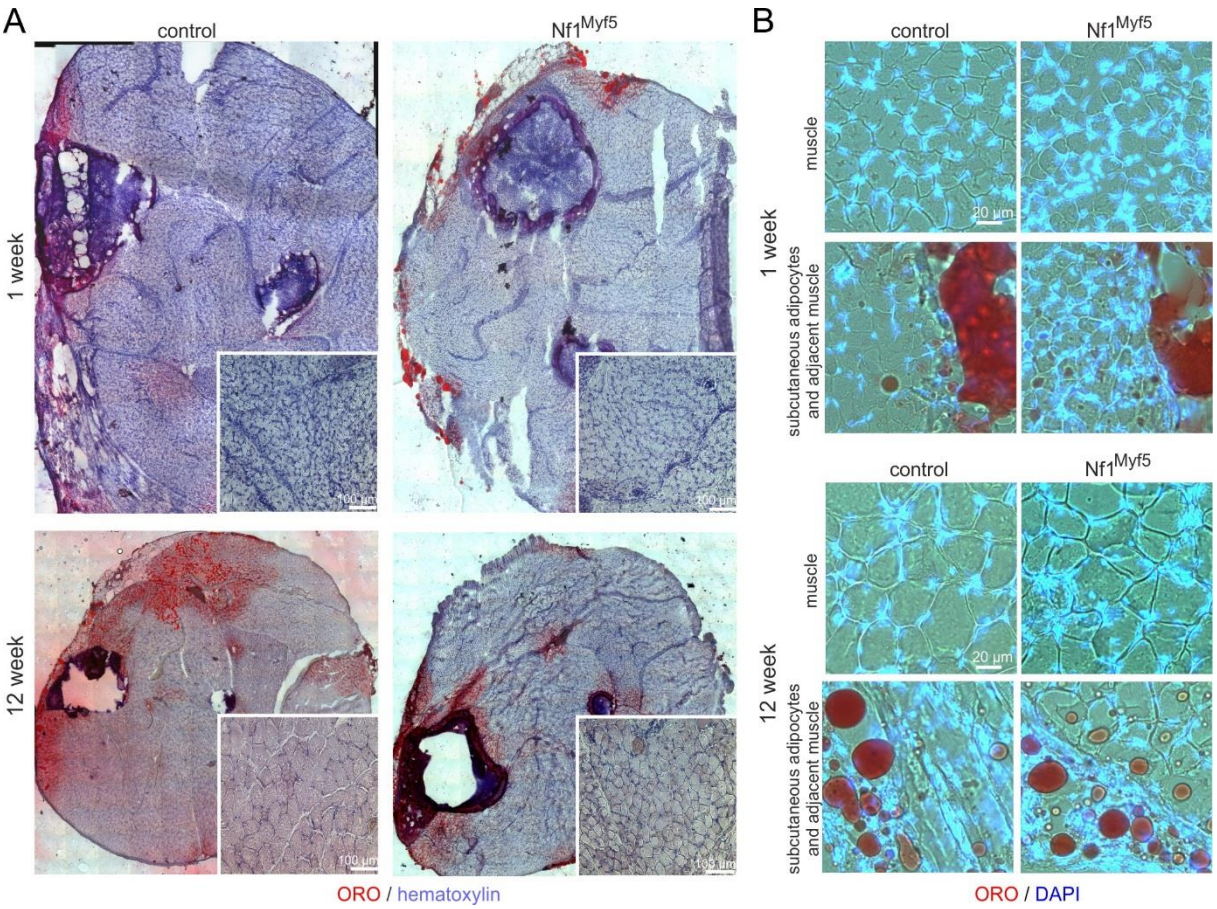


**Fig. S5** Extended data for **lipid metabolism in Nf1$^{Myf5}$ muscle** (A) Hind limb cross sections of 1 week (top) and 12 week (bottom) control and Nf1$^{Myf5}$ mice stained for Oil red O (ORO) and hematoxylin. Oil red O positive muscle-adjacent adipocytes can be seen, frequently lipids smear into the muscle area close to these sites. However the majority of muscle tissue is free of ectopic lipid staining in control and in Nf1$^{Myf5}$ mice **(see inserts). (B) Images of hind limb cross sections of 1 week (top) and 12 week (bottom) control and Nf1$^{Myf5}$ mice stained for Oil red O (ORO) and DAPI imaged with DIC optics. Top row in each panel shows muscle, bottom row shows subcutaneous adipose tissue and adjacent muscle, where lipid droplet artefacts due to smearing can be observed.**

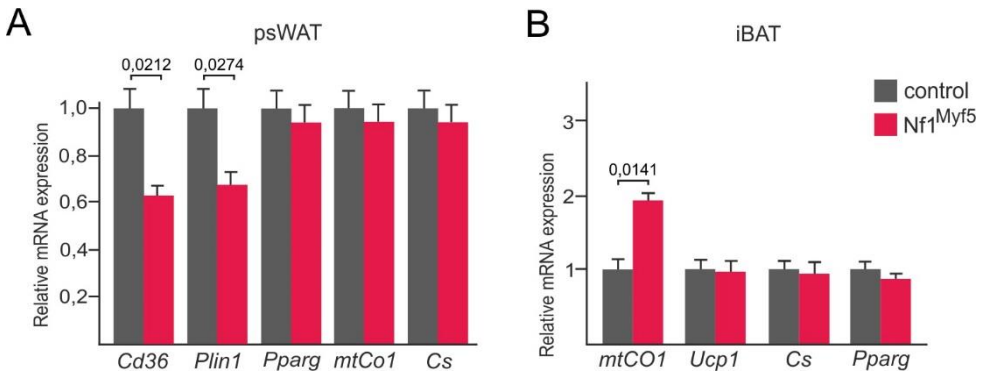


**Fig. S6** Extended data for analysis of adipose tissue in Nf1$^{Myf5}$ mice (**A**) RT-qPCR analysis of psWAT of of 12 week old control vs. Nf1$^{Myf5}$ mice for ***Cd36***, ***Plin1***, *Pparg*, *mtCO1* and *Cs* (n=3 animals per genotype). (**B**) RT-qPCR analysis of interscapular brown adipose tissue (iBAT) of 12 week old control and Nf1$^{Myf5}$ animals for *mtCO1*, *Ucp1*, *Cs* and *Pparg* mRNA (n=3 animals per genotype). **Error bars represent standard error of means (SEM). P-value was calculated by two-sided unpaired t-test.**